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Rheological Changes During the Atrial Fibrillation

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ABSTRACT

BACKGROUND

According to recent estimates atrial fibrillation (AF) affects approximately 1% of the global population with the tendency to grow over the next 50 years. Despite significant advances in the diagnosis and management of AF, it remains one of the biggest challenges for modern medicine.

OBJECTIVES

To better understand of pathological processes underlying AF, we aimed to access relations between hemodynamic and rheological properties of blood in patients with different forms of AF.

METHODS

The erythrocyte (RBC) aggregation index (EAI), erythrocyte (RBC) deformability index EDI), and plasma viscosity (Vpl) were measured in 70 patients with AF and 20 healthy individuals using a textural analysis system (Tas-Plus, Leitz, Germany) and innovative "Georgian technique" with the unique function of a quantitative assessment of the RBC aggregation index.

RESULTS

The mean erythrocyte (RBC) aggregation index (EAI), erythrocyte (RBC) deformability index (EDI), and plasma viscosity (PV) were statistically higher in patients with paroxysmal, persistent, and permanent AF compared to the healthy controls; however, there were no significant differences between different groups of patients with AF.

CONCLUSIONS

The findings of our investigation lead us to believe that disturbances in the hemorheological system play a crucial role in the pathogenesis of AF. These suggest that RBC aggregation is an essential factor in the progression of AF and requires constant monitoring for early prevention and adequate management of the disease.

KEYWORDS

Atrial fibrillation (AF); erythrocyte (RBC) aggregation index (EAI); erythrocyte (RBC) deformability index (EDI); hemorheology; plasma viscosity (PV).

BACKGROUND

Despite all efforts, the prevalence of atrial fibrillation (AF) and associated morbidity and mortality are increasing globally yearly.[1,2] According to the latest evidence, the worldwide incidence of AF is 1%, which is an extremely high number. Moreover, a 2.3-fold increase in incidence is expected due to increased life expectancy and reporting of previously undiagnosed cases.[3,4]

AF is associated with high disability and premature mortality mainly because of ischemic stroke, which is account for 20-30% of all strokes.[5,6] Despite significant advances in the detection and treatment of AF, it remains one of the biggest challenges for modern medicine and requires a multifaceted, multidisciplinary approach to patient management.

There are many hypotheses explaining the pathogenesis of AF, including structural-functional changes in the atrial myocardium that lead to electrophysiological changes, allowing arrhythmias to be detected. In addition, there is a violation of neuro-vegetative control; a re-entry mechanism; possible ionic mechanisms of arrhythmia development, and pathological automatism in the area of the pulmonary vein trunk.[7] All of them entirely or partially rely on focal or small-wave mechanisms but none of them take into account the role of hemodynamical and rheological factors in the development and progression of AF.[8] Hemorheological conditions of the blood are not considered either during the initial diagnosis of the disease or preventive measures and certainly not as a target of treatment. Furthermore, it is not clear which processes occur at the microcirculation level, where the rheological properties of the blood play a crucial role in terms of flow intensity and volumetric velocity.[9] The rheological factors also play an important role in the development of left ventricular hypertrophy, which is one of the main risk factors of AF.[10]

Considering that the adequacy of microcirculation is mainly determined by the rheological properties of the blood, we aimed to access relations between hemodynamic and rheological properties of blood in AF patients, for a better understanding of pathogenesis and optimization of disease management.

METHODS

Patient population

Overall, 70 patients (42 men and 28 women) with an average age of 65±10 years admitted to the Central Republican Hospital (Tbilisi, Georgia) because of various forms of atrial fibrillation (AF) were included in the study after final approvement of the study protocol by local EC and obtaining informed consents from all patients. There was no statistically significant difference between comorbidities. The cases of heart valvular disease, decompensated type 1 diabetes mellitus, and thyroid gland pathologies were excluded.

The patients were distributed among one healthy validation (control) and three development groups based on the type of AF using recommendations of AHA/ACC/HRS and ESC guidelines for atrial fibrillation:[12]

- First development group: 22 patients with a permanent form of atrial fibrillation (12 men and 10 women);
- Second development group: 18 patients with a paroxysmal form of atrial fibrillation (13 men and 5 women);
- Third development group: 10 patients with a persistent form of atrial fibrillation, (7 men and 3 women) and
- Validation (control) group of same average age 20 healthy individuals with normal ECG and no current medication history.

Measurements

Hemorheological parameters such as red blood cell (RBC) aggregation index, RBC deformability, and blood plasma viscosity were monitored in the development and validation cohorts using the textural analysis system (Tas-Plus, Leitz, Germany) and innovative "Georgian technique" with the unique function of a quantitative assessment of the RBC aggregation index.[11,12]

The index of RBC membrane deformability was measured by the nucleopore membrane filter method, which is based on the variation of the RBC exit rate in a porous filter (the 5 µm smallest capillary lumen) under constant pressure.[13,14]

Plasma viscosity was determined at 37.0°C in a capillary viscometer as an average of multiple plasma viscosity measurements.

Besides routine laboratory investigations and 12-lead standard ECG in all patients, 24–48-hour ECG Holter monitoring was used in some patients to identify the paroxysmal variant of atrial fibrillation. Echocardiography was performed according to the updated recommendations of the American Society of Echocardiography.[15]

Statistical analysis

The obtained material was statistically processed with special biostatistical programs: Origin 8.1 (Micro cat Software, Inc.), Biostatistics for Mac (Macintosh), and Microsoft Excel. The final evaluation of the array was done with the IBM SPSS statistical program package (version19.0). Results were expressed as mean ± SD and were considered significant at $p<0.05$.

RESULTS

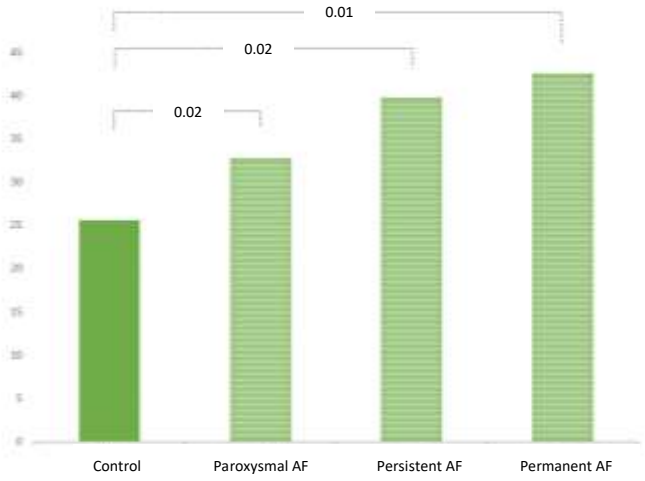
Table 1 represents mean rheological parameters in patients with different forms of AF. The mean erythrocyte (RBC) aggregation index (EAI) was statistically higher in patients with paroxysmal, persistent, and permanent AF compared to the validation (control) group (p=0.02, p=0.02, and p=0.01, respectively); however, there were no significant differences between development groups. The highest mean EAI was in the group of patients with a permanent form of AF (42.6±10.4), and the lowest mean EAI was in the group of paroxysmal AF (32.8± 8.3, p=0.02) (Fig.1).

TABLE 1. The mean rheological parameters in patients with different forms of atrial fibrillation

	EAI	*EDI*	*Vpl*
Paroxismal AF	32.8± 9.4	2.29±0.03	1.18±0.07
Persistent AF	39.8±13.8	2.18±0.04	1.18±0.08
Permanent AF	42.6±10.4	27.81 ± 0.09	1.20±0.07
Control	25.6±1.29	2.17±0.02	1.09±0.04

Abbreviations: AF: atrial fibrillation; EAI: erythrocyte (RBC) aggregation index; EDI: erythrocyte (RBC) deformability index; Vpl: plasma viscosity.

FIGURE 1. Erythrocyte (RBC) aggregation index (EAI) in patients with different forms of atrial fibrillation



The mean erythrocyte (RBC) deformability indexes (EDIs) were statistically higher in all development groups compared to control (p=0.01, p=0.02, and p=0.01 for paroxysmal, persistent, and permanent AF patients, respectively), with highest indices in the group of patients with permanent AF (2.27±0.02) and lowest in the group of patients with persistent AF (2.20±0.05) (Fig.2). There were no significant differences between the groups of patients with AF.

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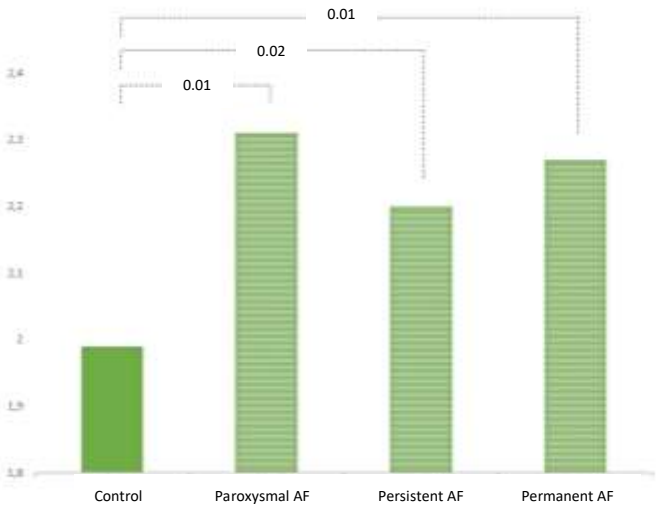
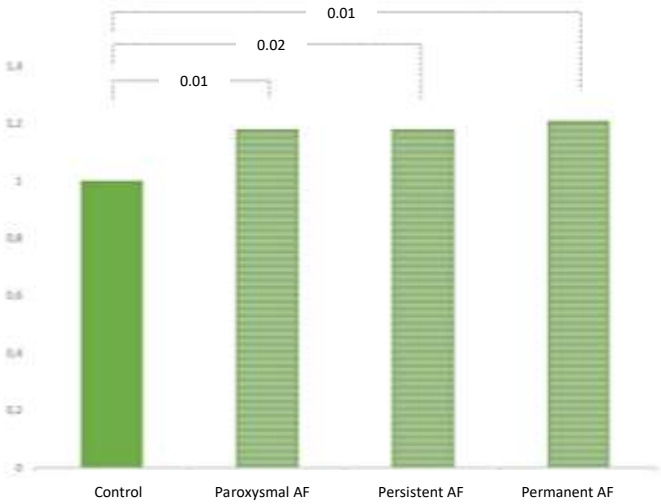
FIGURE 2. Erythrocyte (RBC) deformability index (EDI) in patients with different forms of atrial fibrillation



The mean plasma viscosity (VP) indices were statistically higher in all development groups compared to healthy control (p=0.01, p=0.02, and p=0,01 for paroxysmal, persistent, and permanent AF patients, respectively), without significant differences between different forms of AF (Fig.3).

FIGURE 3. Plasma viscosity (Vpl) in patients with different forms of atrial fibrillation



DISCUSSION

Despite achievements in the study of the pathogenesis of atrial fibrillation (AF), and its management, the number of patients suffering from AF is increasing rather than decreasing, and AF remains one of the major risk factors for ischemic stroke.[16-19]

The growing scientific interest regarding rheological factors in the pathogenesis of cardiovascular diseases indicates their crucial role in chronic ischemic heart disease and arterial hypertension. For example, an increase in the RBC aggregation index is suggested as a predictor of coronary artery disease.[20-30]

In the present study, blood rheological parameters were studied in patients with AF for the first time in Georgia using the innovative and widely acknowledged "Georgian technique" for the assessment of red blood cell (RBC) aggregability.[20-30]

We discovered a link between the progression of AF and negative changes in blood rheological parameters. As is well known, hemorheological and hemodynamic factors play a crucial role in the maintenance of optimal perfusion and proper function of the myocardium as well as any other tissue. In the case of AF, special attention is paid to the different structural, functional, and electrophysiological changes of the atrial myocardium, depending on the type of AF.

The findings of our investigation lead us to believe that disturbances in the hemorheological system are at the root of the pathophysiology and severity of atrial fibrillation. Increased erythrocyte aggregation leads to the gain of peripheral resistance, which in association with irregular contractility of the left ventricle (LV), aggravates LV dysfunction and thus forms favorable conditions for the maintenance of AF.

According to our findings, blood rheological changes occur at the earliest stage of AF. The aggregation ability of RBCs, the powerful determinant of rheological changes, increases following disease progression. The rheological changes expressed during paroxysmal AF deepen in the case of the persistent and permanent types of the disease. The increased RBC aggregation and plasma viscosity aggravate existing dramatic thrombogenic changes and contribute rapid progression of AF.

These findings suggest that RBC aggregation is an important factor in the progression of AF and requires constant monitoring for early prevention and adequate management of the disease. The "Georgian technique" used in the present study allowed us to obtain accurate quantitative data and seems to be ideal for the ongoing control of blood rheological parameters, elaboration of personalized therapeutic strategies, and prevention of non-fatal/fatal complications of AF.

The main limitation of our study is the small sample size, which may have influenced the results.

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